

**REMARKS**

Favorable reconsideration of this application, in light of the preceding amendments and following remarks, is respectfully requested.

Claims 1, 2, 5-8, 11, 12, 17, 19-21, and 24-30 are pending in this application. Claims        are amended and claims        have been cancelled. Claims 1, 17, 24 and 29 are the independent claims.

**Specification Objections**

The Examiner states that paragraph 36 of present specification contains a sequence larger than 10 nucleotides but lacks an appropriate SEQ ID TAG. As the nucleotide sequence on paragraph 36 is the same sequence shown as SEQ ID NO: 1, Applicants have amended the specification accordingly. Therefore, withdrawal of the objection to the specification is respectfully requested.

**Example Embodiments of the Present Application**

Example embodiments recite a method of modulating immunological activities comprising orally administering fungal immunomodulatory protein or protein fused with FIP to a subject, wherein the fungal immunomodulatory protein is encoded by a nucleic acid molecule including SEQ. ID NO. 1. Example non-limiting embodiments of this feature are discussed, for example, in sections 8, 9 and 73, and FIGS. 1 and 2 of the instant specification.

As we can see in sections 8 and 9 of the present specification, the SEQ. ID No. 1 has advantages such as efficiently using fungi to produce the fungal immunomodulatory protein (FIP). The conventional method of producing FIP is time-consuming and costly. Yeast is used to produce the FIP in example embodiments, because (a) the yeast and Ling-Zhi both belong to the fungi species, and (b) yeast is

safe for direct oral administration without an extraction and purification process. However, when integrating the wild type Ling-Zhi-8 nucleotide codon into yeast, the FIP producing rate is not satisfied and not suitable for massive production, because of the inclination of yeast for a specific codon. Thus, the wild type Ling-Zhi-8 nucleotide codon has been modified in SEQ ID NO. 1 to include the codon that was better expressed in fungi based on its high tRNA translation efficiency.

Further, as seen in example 3, section 73 of the present specification, the improved FIP nucleotide codon, SEQ ID NO:1, can be highly expressed in yeast compared to the original wild type Ling-Zhi-8 nucleotide codon in yeast. After the modification of FIP codon, the FIP can be produced in yeast with better efficiency, and commercial production can be improved.

#### **Rejections under 35 U.S.C. § 102**

Claims 29-30 rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Evans et al (US Patent Number 5,928,896, hereinafter "Evans") in light of Murasugi et al. (Journal of Biological Chemistry Vol. 256, No.4, pp2486-2593, 1991, hereinafter "Murasugi"). Applicants respectfully traverse this rejection for the reasons detailed below.

The Examiner states that Evans discloses compositions of immunomodulatory peptides comprising Ling-Zhi-8 for oral administration. The Examiner also asserts that Murasugi discloses the amino acid sequence of Ling-Zhi-8, and the amino acid sequence is 100% identical to SEQ ID NO:1. Applicants respectfully disagree for the reasons stated below.

First, the **nucleotide** SEQ ID NO:1 as recited in claim 29 is NOT the same as the **amino acid** sequence disclosed in Murasugi, even though SEQ ID NO: 1 will decode the same amino acid as Murasugi. The nucleotide sequence of SEQ ID NO:1 is

modified and not the same as the wild type Ling-Zhi-8 nucleotide codon, but can decode the same amino acid as wild type Ling-Zhi. The SEQ ID NO: 1 and SEQ ID NO: 2 are listed below, respectively. The different codon sites have been highlighted.

**SEQ ID NO:1 (Modified FIP nucleotide codon)**

ATGTCTGATA CTGCTTTGAT TTTCAGATTG GCTTGGGATG TTAAGAAGTT  
GTCTTTCGAT TACTCTCCAA ACTGGGGTAG AGGTAACCCA AACAACTTCA  
TTGATACTGT TACTTTCCCA AAGGTTTTGA CTGATAAGGC TTACACTTAC  
AGAGTTGCTG TTTCTGGTAG AAAGTTGGGT GTTAAGCCAT CTTACGCTGT  
TGAATCTGAT GGTTCTCAA AGGTAACTT CTTGGAATAC AACTCTGGTT  
ACGGTATTGC TGATACTAAC ACTATTCAAG TTTTCGTTGT TGATCCAGAT  
ACTAACAACG ATTCATTAT TGCTCAATGG AACTGA

**SEQ ID NO: 2 (Original wild type Ling-Zhi-8 nucleotide codon)**

ATGTCCGACA CTGCCTTGAT CTTCAGGCTC GCCTGGGACG TGAAGAAGCT  
CTCGTTCGAC TACACCCCGA ACTGGGGCCG CGGCAACCCC AACAACTTCA  
TCGACACTGT CACCTTCCCG AAAGTCTTGA CCGACAAGGC GTACACGTAC  
CGCGTCGCCG TCTCCGGACG GAACCTCGGC GTGAAACCCT CGTACGCGGT  
CGAGAGCGAC GGCTCGCAGA AGGTCAACTT CCTCGAGTAC AACTCCGGGT  
ATGGCATAGC GGACACGAAC ACGATCCAGG TGTTTCGTTGT CGACCCCGAC  
ACCAACAACG ACTTCATCAT CGCCCAGTGG AACTAG

As shown above, the SEQ ID NO:1 has several different codons compared with SEQ ID NO:2 (Ling-Zhi-8 nucleotide codon), and one skilled in the art would understand that the Ling-Zhi-8 amino acid sequence of Murasugi is different from a nucleotide sequence as recited in claim 29.

Therefore, Applicants submit that the nucleotide sequence (not the amino acid sequence) of Murasugi does not correspond with SEQ ID NO:1 as recited in claim 29, and as such does not render obvious claim 29.

Claim 30, dependent on independent claim 29, is patentable for the reasons stated above with respect to claim 29 as well as for its own merits.

The Applicants, therefore, respectfully request that the rejection to Claims 29-30 under 35 U.S.C. § 102(b) or in the alternative, under 35 U.S.C. § 103(a) be withdrawn.

**CONCLUSION**

In view of the above remarks and amendments, the Applicants respectfully submit that each of the pending objections and rejections has been addressed and overcome, placing the present application in condition for allowance. A notice to that effect is respectfully requested. If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to contact the undersigned.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Erin G. Hoffman, Reg. No. 57,752, at the telephone number of the undersigned below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 08-0750 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

HARNESS, DICKEY, & PIERCE, P.L.C.

By

\_\_\_\_\_  
John A. Castellano, Reg. No. 35,094  
P.O. Box 8910  
Reston, Virginia 20195  
(703) 668-8000

JAC/EGH:has  
1186263.1